Pancreatic secretions From Exocrine part

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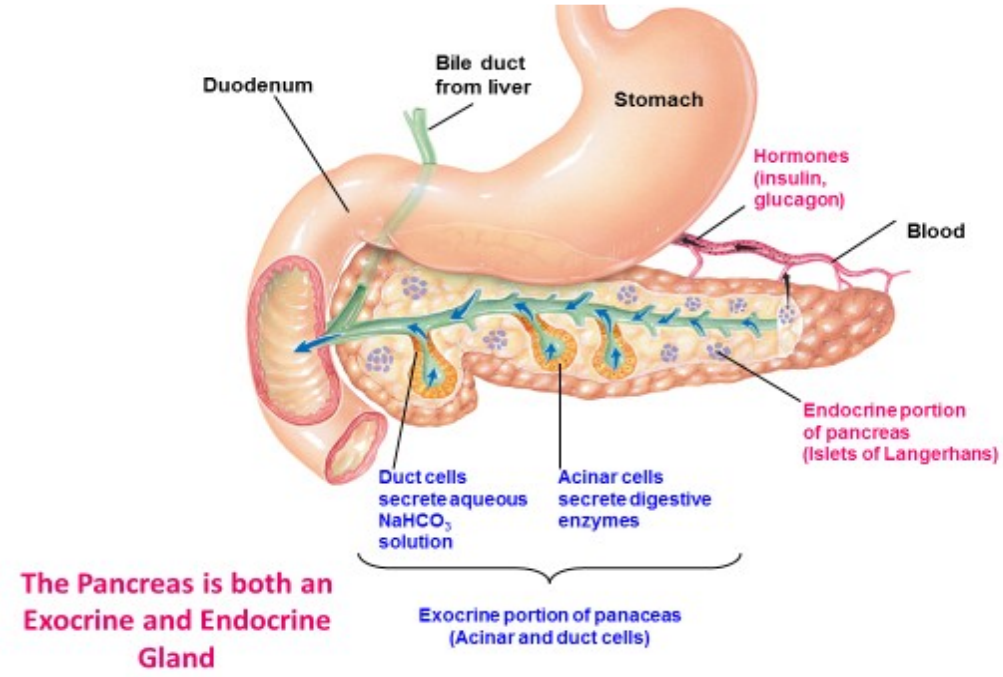
ILOs

By the end of this lecture the student will be able to:

1. Describe the composition of the exocrine pancreas.
2. List the most important pancreatic digestive enzymes.
3. Explain their functions in digestion.
4. Explain the mechanism by which pancreatic secretion is regulated.
5. Apply knowledge to solve clinical problem.



Pancreas has 2 functions:

a) Endocrine functions: secretes insulin, glucagon, ... from islets of Langerhans.

b) Exocrine function: Acini are the exocrine secretory units → secretion of pancreatic juice, which pass in pancreatic duct to Small intestine, it has 2 components: aqueous and enzymatic components.

Properties and functions of pancreatic secretion:

Volume: 1-2 L /day (≈ 1500 mL). pH: 8 (alkaline)

Composition:

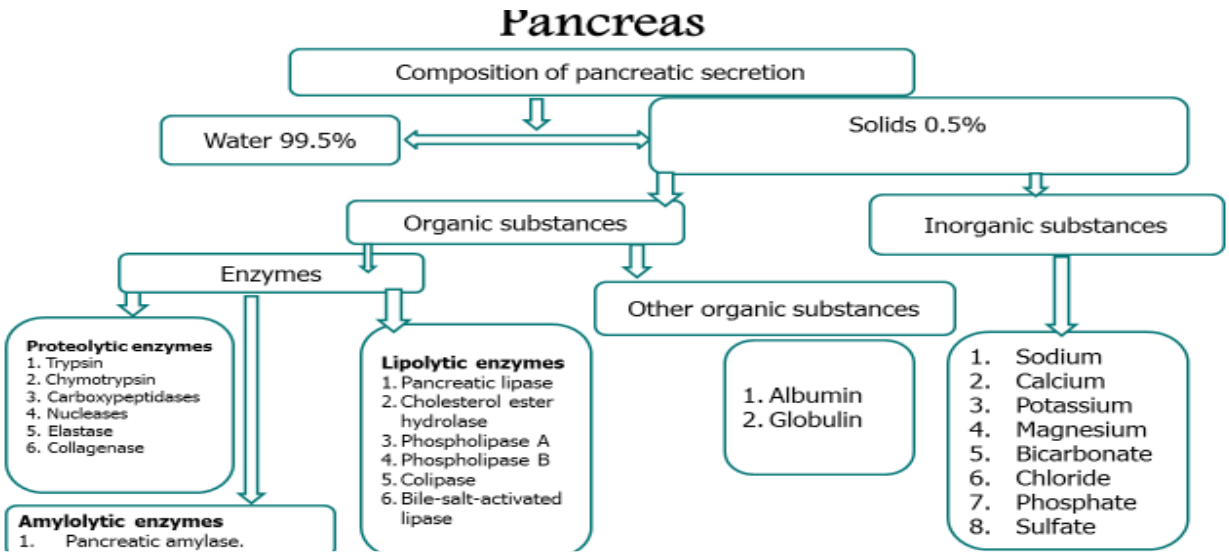
A. Aqueous alkaline component, Secreted by the duct cells. Rich in $HCO3^-$ ($HCO3^-$ content approximately 113 mEq/L vs. 24 mEq/L in plasma), that is important for **neutralizing** stomach acid in the duodenum so → 1. Protect duodenal mucosa.

2. Provides optimum medium for action of pancreatic enzymes → can function properly.

N.B.: Bile and intestinal juices are also neutral or alkaline, and these three secretions neutralize the gastric acid……., raising the pH of the duodenal contents to 6.0 - 7.0.

B. Enzymatic component is essential for the **proper digestion** and absorption of carbohydrates, fats, and proteins.

So, Pancreatic juice has digestive functions and neutralizing action.

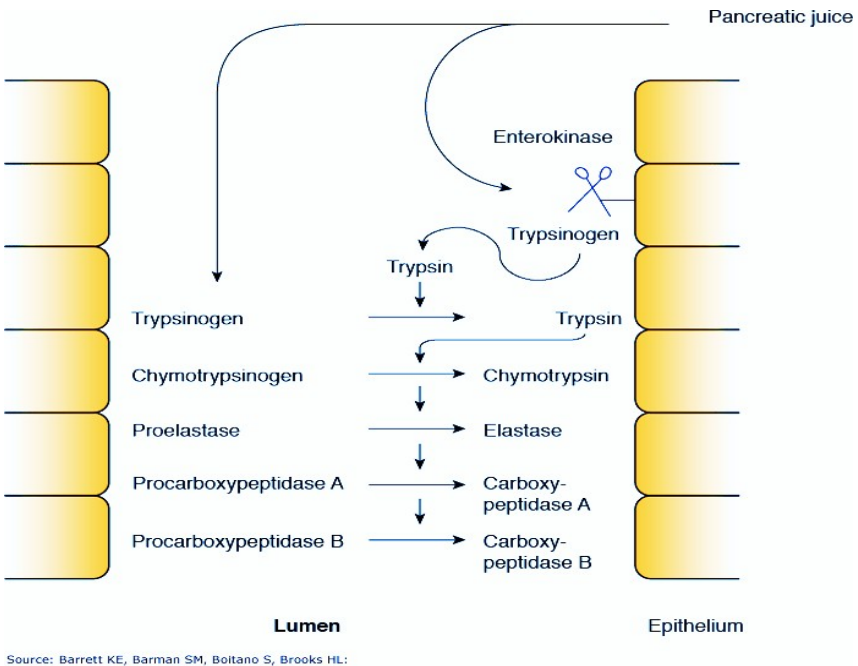


Digestive enzymes of pancreatic juice and their actions

- Pancreatic juice plays an important role in the digestion of proteins and lipids. It also has mild digestive action on carbohydrates.
- So, Pancreatic juice contains enzymes for digesting proteins, carbohydrates and fats.
- Pancreatic enzymes are *fully sufficient for complete digestion* even in the absence of salivary amylase and gastric pepsin.

Digestion of protein, Major Proteolytic enzymes of pancreatic juice are trypsin and chymotrypsin. Other proteolytic enzymes are carboxypeptidases (carboxypeptidase A and carboxypeptidase B.), nucleases (ribonuclease and deoxy ribonuclease), elastase and collagenase.

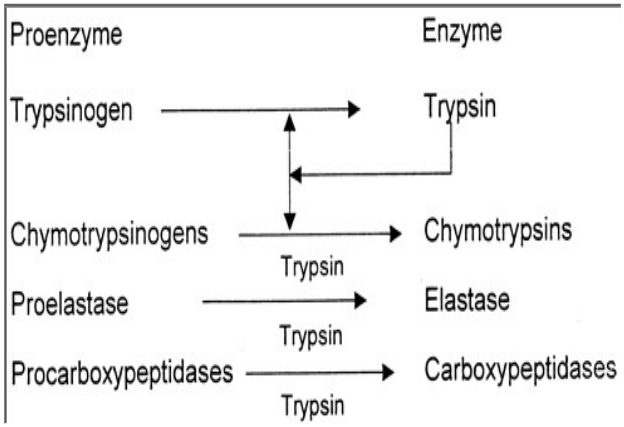
- Trypsin and chymotrypsin are endopeptidases that break peptide bonds within the protein molecule. Thus, they split whole and partially digested proteins into peptides of various sizes, but do not release individual amino acids.
- Carboxypeptidase is an exopeptidase that breaks the ends of the protein molecule. It splits individual amino acids from the carboxyl ends of the peptides, thus completing the digestion of most proteins into amino acids. The nucleases split the two types of nucleic acids.
- The proteolytic enzymes of the pancreas are secreted as inactive form "proenzymes".
- When the pancreatic juice enters the duodenum, trypsinogen is converted to the active



Source: Barrett KE, Barman SM, Boitano S, Brooks HL:

enzyme trypsin by the brush border enzyme enteropeptidase (enterokinase).

- The secretion of enteropeptidase is increased by cholecystokinin (CCK).
- Trypsin converts chymotrypsinogens into chymotrypsins and other proenzymes.
- Trypsin can also activate trypsinogen; therefore once some trypsin is formed, there is an autocatalytic chain reaction.



Activation of the pancreatic proteolytic enzymes in the duodenum. An example of a rapid and complete positive feedback.

- There is a potential danger of the release of a small amount of trypsin into the pancreas which produce active enzymes that could digest the pancreas.

So, pancreas must protect itself from digestion "auto digestion" by its proteolytic enzymes. How?

1. Proteolytic enzymes remain inactive until they reach duodenum "zymogen granules are formed in the cell and discharged by exocytosis from the apexes of the cells into the lumens of the pancreatic ducts".
2. Fortunately, the same cells that secrete the proteolytic enzymes into the acini of the pancreas secrete simultaneously another substance called trypsin inhibitor, which prevents activation of trypsin both inside the secretory cells and in the acini and ducts of the pancreas.
3. Trypsin inhibitor inhibits trypsin activation and so on inhibits activation of many other zymogens (also digest dietary protein) to their active form.

N.B.:

- ♥ Enteropeptidase deficiency occurs as a congenital abnormality and leads to protein malnutrition.
- ♥ When there is severe damage of the pancreas or blockage of the duct, large quantities of pancreatic secretions accumulate in the damaged areas of the pancreas, and the pancreatic secretions become rapidly activated and attack the pancreas.
- ♥ Also phospholipase A2 is activated in the pancreatic ducts, with the formation of lyso -Phosphatidylcholine from the phosphatidylcholine that is a normal constituent of bile. This causes disruption of pancreatic tissue and necrosis of surrounding fat.
- ♥ Pancreatitis is the inflammation of pancreatic acini. It is a rare but dangerous disease.
- ♥ Pancreatitis may be acute or chronic.

Digestion of lipids, Lipolytic enzymes present in pancreatic juice are pancreatic lipase, cholesterol ester hydrolase, phospholipase A_2, ..., colipase and bilesaltactivated lipase.

Digestion of carbohydrates, Pancreatic amylase is the amylolytic enzyme present in pancreatic juice. It converts starch into dextrin and maltose.

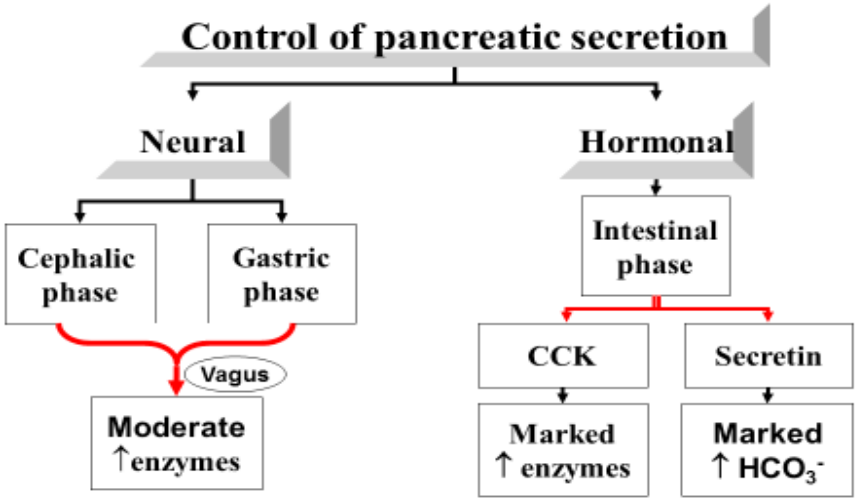
N.B.: Most carbohydrates are ingested as starch- a polymer of glucose. Salivary amylase begins starch digestion. Pancreatic amylase converts starch to oligosaccharides. Small intestine brush border enzymes hydrolyze oligosaccharides

N.B.:

- ♥ Pancreatic **Amylase** and **lipase** secreted in the active form.
- ♥ Small amounts of pancreatic digestive enzymes normally leak into the circulation, but in acute pancreatitis, the circulating levels of the digestive enzymes rise markedly. Measurement of the plasma

amylase or lipase concentration is therefore of value in diagnosing pancreatitis.

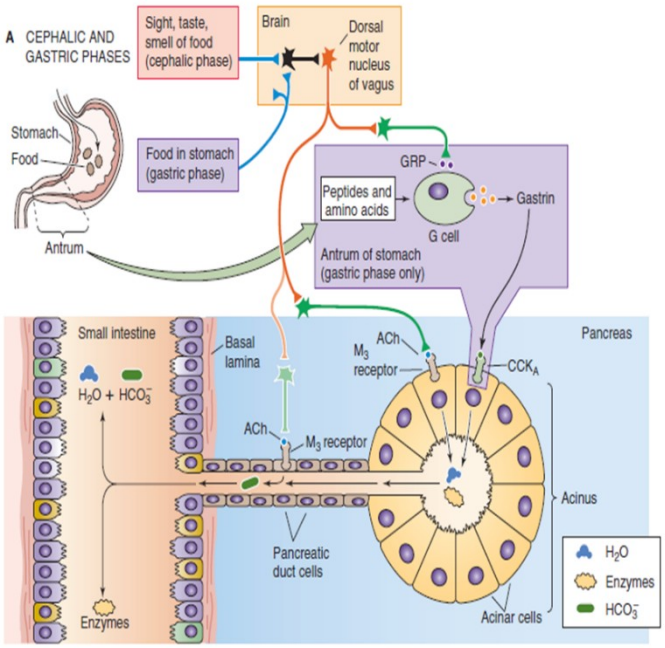
Control of pancreatic secretions



It is primarily under hormonal control.

Nervous control of pancreatic secretion ??? %

- *During cephalic phase*, both conditioned & unconditioned Reflexes (thinking of, sight or smelling food, food in mouth, chewing, ...) → Parasympathetic impulses along vagus



nerves stimulate secretion of a **small amount** of pancreatic juice **rich in enzymes**.

- Acetylcholine acts on acinar cells via phospholipase C → secretion of zymogen granules.
- *During gastric phase,* "when food enters the stomach" gastrin is secreted from stomach → transported to pancreas through blood → stimulates the pancreatic secretion rich in enzymes.

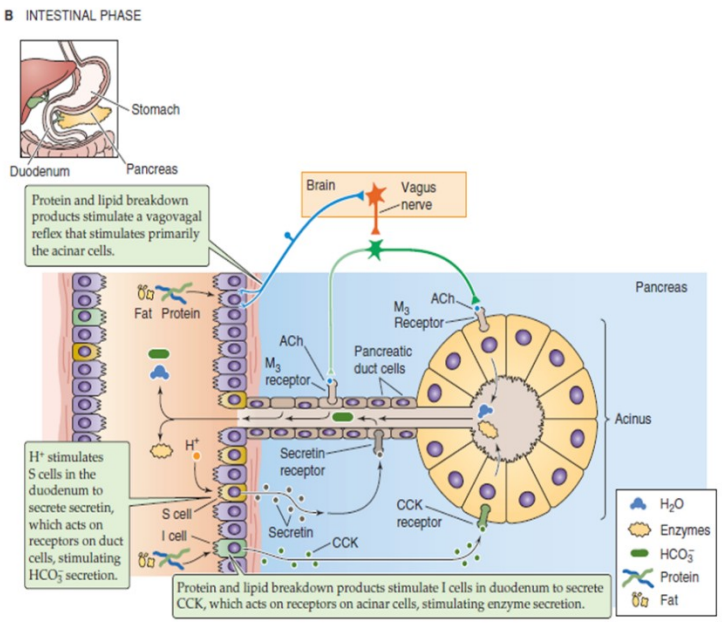
N.B.: Gastric phase " combined ??????????????????"

- Cephalic and gastric phase → (weak effect).

Hormonal Regulation *of Pancreatic Secretion* **"Primarily"**

??? % during intestinal phase.

Secretin: Occurs in response to acid chyme in duodenum "duodenal pH < 4.5".



- Stimulates copious secretion" from duct cell" of a very alkaline pancreatic juice rich in HCO_3^- but poor in enzymes.
- Stimulates the liver to secrete bile secretion rich in $HC0_3^-$.
- The effect on duct cells is due to an increased intracellular cyclic AMP.

CCK: Occurs in response to the presence of digestive products of fat and protein "content of chyme" in duodenum.

- Acts on the acinar cells to cause the release of zymogen granules and production of pancreatic juice rich in enzymes but low in volume.
- It acts like acetylcholine by activating phospholipase C
- Enhances secretin.
- Relaxation of the sphincter of Oddi. On Gall bllader.....

N.B.: * Both hormones are secreted by upper intestinal cells.

* *Gastrin* from stomach and duodenum weakly stimulates gallbladder contraction and pancreatic enzyme secretion.

N.B.:

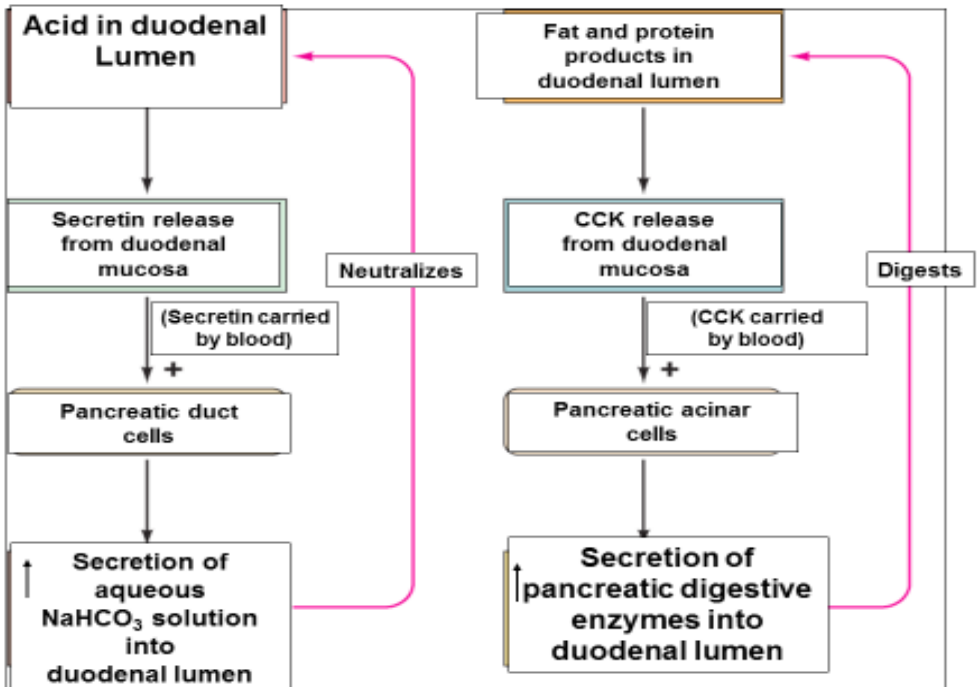
*Deficiency of pancreatic enzymes → Steatorrhea → Excessive undigested fat in feces.

*Blocking Pancreatic Duct→ decrease pancreatic lipase→ Failure of fat digestion→ Steatorrhea.

*Failure of Fat digestion & absorption→ Failure of absorption of fat soluble vitamins e.g.

- Vitamin D→ Vitamin D deficiency → decrease absorption of Ca^{++}
- Vitamin K → Vitamin K deficiency → Increased bleeding tendency.
- Vitamin A→ .....
  →.....
- Vitamin E→ .....
  →.....

The following figure shows control of pancreatic secretions



Digestive enzymes of Pancreas

Source	Enzyme	Activator	Substrate	Catalytic Function or Products
Exocrine Pancreas	Trypsin (trypsinogen)	Enteropeptidase	Proteins and polypeptides	Cleave peptide bonds on carboxyl side of basic amino acids (arginine or lysine)
	Chymotrypsins (chymotrypsinogens)	Trypsin	Proteins and polypeptides	Cleave peptide bonds on carboxyl side of aromatic amino acids
	Elastase (proelastase)	Trypsin	Elastin, some other proteins	Cleaves bonds on carboxyl side of aliphatic amino acids
	Carboxypeptidase A (procarboxypeptidase A)	Trypsin	Proteins and polypeptides	Cleave carboxyl terminal amino acids that have aromatic or branched aliphatic side chains
	Colipase (procolipase)	Trypsin	Fat droplets	Facilitates exposure of active site of pancreatic lipase
	Pancreatic lipase	. . .	Triglycerides	Monoglycerides and fatty acids
	Cholesteryl ester hydrolase	. . .	Cholesteryl esters	Cholesterol+ fatty acid

	Bile salt-acid lipase		Cholesteryl esters	Cholesterol
	Pancreatic α -amylase	Cl–	Starch	Hydrolyzes 1:4 α linkages, producing α -limit dextrins, maltotriose, and maltose
	Ribonuclease	. . .	RNA	Nucleotides
	Deoxyribonuclease	. . .	DNA	Nucleotides
	Phospholipase A_2 (pro-phospholipase A_2)	Trypsin	Phospholipids	Fatty acids, lysophospholipids

SUGGESTED TEXTBOOKS

1. Ganong's "Review of Medical Physiology".
2. Guyton and Hall "Textbook of Medical Physiology".
3. Sembulingam "Essentials of Medical Physiology".